carbamoyl phosphate synthetase I deficiency

Carbamoyl phosphate synthetase I deficiency is an inherited disorder that causes ammonia to accumulate in the blood (hyperammonemia). Ammonia, which is formed when proteins are broken down in the body, is toxic if the levels become too high. The brain is especially sensitive to the effects of excess ammonia.

In the first few days of life, infants with carbamoyl phosphate synthetase I deficiency typically exhibit the effects of hyperammonemia, which may include unusual sleepiness, poorly regulated breathing rate or body temperature, unwillingness to feed, vomiting after feeding, unusual body movements, seizures, or coma. Affected individuals who survive the newborn period may experience recurrence of these symptoms if diet is not carefully managed or if they experience infections or other stressors. They may also have delayed development and intellectual disability.

In some people with carbamoyl phosphate synthetase I deficiency, signs and symptoms may be less severe and appear later in life.

Frequency

Carbamoyl phosphate synthetase I deficiency is a rare disorder; its overall incidence is unknown. Researchers in Japan have estimated that it occurs in 1 in 800,000 newborns in that country.

Genetic Changes

Mutations in the *CPS1* gene cause carbamoyl phosphate synthetase I deficiency. The *CPS1* gene provides instructions for making the enzyme carbamoyl phosphate synthetase I. This enzyme participates in the urea cycle, which is a sequence of biochemical reactions that occurs in liver cells. The urea cycle processes excess nitrogen, generated when protein is broken down by the body, to make a compound called urea that is excreted by the kidneys. The specific role of the carbamoyl phosphate synthetase I enzyme is to control the first step of the urea cycle, a reaction in which excess nitrogen compounds are incorporated into the cycle to be processed.

Carbamoyl phosphate synthetase I deficiency belongs to a class of genetic diseases called urea cycle disorders. In this condition, the carbamoyl phosphate synthetase I enzyme is at low levels (deficient) or absent, and the urea cycle cannot proceed normally. As a result, nitrogen accumulates in the bloodstream in the form of toxic ammonia instead of being converted to less toxic urea and excreted. Ammonia is especially damaging to the brain, and excess ammonia causes neurological problems and other signs and symptoms of carbamoyl phosphate synthetase I deficiency.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- carbamoyl-phosphate synthase I deficiency disease
- carbamyl-phosphate synthetase I deficiency disease
- congenital hyperammonemia, type I

Diagnosis & Management

Formal Treatment/Management Guidelines

- New England Consortium of Metabolic Programs: Acute Illness Protocol
  http://newenglandconsortium.org/for-professionals/acute-illness-protocols/urea-cycle-disorders/carbamyl-phosphate-synthetase-deficiency-cps/

Genetic Testing

- Genetic Testing Registry: Congenital hyperammonemia, type I
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0751753/

Other Diagnosis and Management Resources

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/carbamoyl-phosphate-synthetase-i-deficiency
- GeneReview: Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217
- MedlinePlus Encyclopedia: Hereditary Urea Cycle Abnormality
  https://medlineplus.gov/ency/article/000372.htm
- National Organization for Rare Disorders (NORD) Physician Guide: Urea Cycle Disorders
  http://nordphysicianguides.org/urea-cycle-disorders/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html

- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Hereditary Urea Cycle Abnormality
  https://medlineplus.gov/ency/article/000372.htm
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Metabolic Disorders
  https://medlineplus.gov/metabolicdisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Carbamoyl phosphate synthetase 1 deficiency
  https://rarediseases.info.nih.gov/diseases/7269/carbamoyl-phosphate-synthetase-1-deficiency

Educational Resources

- Disease InfoSearch: Congenital hyperammonemia, type I
  http://www.diseaseinfosearch.org/Congenital+hyperammonemia%2C+type+I/8065
- Genetics Education Materials for School Success (GEMSS)
  http://www.gemssforschools.org/conditions/urea-cycle/default
- Orphanet: Carbamoyl-phosphate synthetase 1 deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=147

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/carbamoyl-phosphate-synthetase-i-deficiency/

- National Urea Cycle Disorders Foundation
  http://www.nucdf.org/
- Urea Cycle Disorders Consortium
  http://www.rarediseasesnetwork.org/cms/ucdc/Learn-More/Disorder-Definitions

GeneReviews

- Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22carbamoyl+phosphate+synthetase+I+deficiency%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28carbamoyl+phosphate+synthase+1+deficiency%5BALL%5D%29+OR+%28cps1+deficiency%5BALL%5D%29+OR+%28carbamoyl+phosphate+synthetase+1+deficiency%5BALL%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- CARBAMOYL PHOSPHATE SYNTHETASE I DEFICIENCY, HYPERAMMONEMIA DUE TO
  http://omim.org/entry/237300

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Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/carbamoyl-phosphate-synthetase-i-deficiency

Reviewed: February 2013
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services